REMARKS

Claims

Claims 74 and 76–84 have been elected for prosecution herein pursuant to the restriction requirement of June 23, 2008.

Claims 1–73 were previously cancelled. Claim 75 is hereby cancelled without prejudice or disclaimer. Applicants reserve the right to re-introduce cancelled subject matter during prosecution.

The allowability of claim 76 is gratefully acknowledged.

Claim amendments

Claim 74 incorporates the subject matter of claim 75, which is hereby cancelled without prejudice or disclaimer. Amended claim 74 is further supported by the disclosure contained in, for example, paragraphs [0023] and [0031] of the published specification (US publication No. 2006-0251668).

Claim 79 has been amended to use language in accordance with conventional US practice.

Amended claims 81 and 84 are supported by the disclosure contained in, for example, the paragraph bridging pages 43 and 44 of the originally-filed application.

It is respectfully submitted that the amendments do not raise new matter. Entry thereof is earnestly solicited.

Exhibit

Exhibit A, containing experimental data on the characterization of the recognition molecules of the present invention, is enclosed herewith. Consideration thereof is respectfully requested.

Rejection under 35 U.S.C. §112, ¶2

The rejection of claim 76 for alleged lack of antecedent basis is rendered moot by the forgoing amendments.

Applicants disagree with the PTO's contention that recitation of MHC class I antigen in claim 79 renders it indefinite. The claim terms "MHC class I antigen" and "MHC class II antigen" were well-recognized in the art as of the earliest priority date of the present application. For example, a search on PUBMED reveals 425 articles on MHC class I antigens and 581 articles on MHC class II antigens, all of which were published before the earliest priority date of the present application (November 29, 2002). Thus, it is clear that the "antigen" (i.e., MHC class I or II antigen) is the MHC class I or II molecule as such, whose structures and properties were well-recognized by

a skilled immunologist. See, *Capon v. Eshhar v. Dudas*, (Fed. Cir. 2005) 418 F.3d 1349, 76 U.S.P.Q.2d 1078 (discussed *infra*). Accordingly, for a skilled artisan who is in possession of the references and recognizes the structures and biological properties of such molecules, "MHC class I (or class II) antigen" as used herein is not an arbitrary name but a name for a well-characterized protein.

Moreover, it is by now well-settled that "The requirement to 'distinctly' claim means that the claim must have a meaning discernible to one of ordinary skill in the art when construed according to correct principles. Only when a claim remains insolubly ambiguous without a discernible meaning after all reasonable attempts at construction must a court declare it indefinite." See *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1366, 71 USPQ2d 1081, 1089 (Fed. Cir. 2004) and MPEP §2173.02. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. §112, ¶1 (enablement)

Reconsideration of the rejections made in the Office Action of February 19, 2009 is respectfully requested.

(a) Claims directed to recognition molecules

At the outset, it is respectfully submitted that the lack of enablement rejection with respect to the claimed structure(s) of the recognition molecules of the present invention is moot in view of the aforementioned arguments and/or amendments. The recognition molecules are now claimed as comprising *the CDR regions* that mediate antigen binding. No agreement is to be implied.

(b) Claims directed to constructs comprising the recognition molecules

The Office Action alleges that the claimed constructs, which are taught by the specification to comprise molecules that are fused, chemically coupled, covalently or non-covalently associated with the recognition molecules of the present invention are non-enabled in that the specification does not provide adequate guidance as to how to make and use such constructs. Applicants respectfully disagree.

Enclosed are references which demonstrate that making and using of the constructs of the present invention was routine in the art as of the earliest priority date of the present application. To this end, Chames et al. (*FEMS Microbiology Letters*, 89, pp. 1-8, 2000) disclose that recognition molecules, such as antibodies, could be engineered, for example, by standard genetic manipulation techniques. King et al., (*Cancer Res.* 54, pp. 6176-6185, 1994) show that antibodies can be chemically cross-linked with, for example, radioactive labels (see Abstract). Kuan et al. (*Proc. Natl. Acad. Sci.* 93, pp. 974-978, 1996) describe a recognition molecule fused with a Pseudomonas exotoxin (see

Abstract). Lunde et al. (*Biochem. Soc. Trans.* 30, pp. 500-506, 2000) describe the synthesis and use of troy-bodies and pep-bodies which have the ability to bind antibody effector molecules. Further guidance is also available through standard antibody engineering textbooks, such as, for example, "Antibody Engineering" edited by Kontermann and Dribel.

(c) Claims directed to method of use

The Office Action alleges that the method claims directed to preventing, diagnosing, reducing, treating, following-up and/or after-caring tumor diseases or metastasis are non-enabled. At the outset, Applicants submit that the aforementioned end uses are directed to diagnosing, reducing, treating, following-up and/or after-caring core-1 positive tumors and metastasis thereof. Applicants' amendment of the claims is not to be construed with acquiescence to this or any other ground of rejection.

Secondly, the Examiner argues that it is not credible that a recognition molecule of the invention is able to be effective in treating a tumor, since, for example, no ADCC is shown for the claimed recognition molecule. This contention and the enablement rejection based thereon are respectfully traversed. Insofar as that the Office Action fails to present any evidence which suggests the uses are not enabled, the rejection is deficient under controlling case law.

The burden is upon the Patent and Trademark Office to provide evidence shedding doubt that the invention can not be made and used as stated; see for example, *In re Marzocchi*, 439, F. 2d 220, 169 USPQ 367 (CCPA 1971). Moreover, Applicants' specification teaches that recognition molecules of the present invention are useful for practicing the methods claimed herein. See, for example, paragraph [0009] of the published application. In this regard, Applicants' specification expressly teaches that core-1 antigens are involved in the etiology of tumors and that recognition molecules directed thereto can be used in the diagnosis and treatment of such tumors. See, paragraphs [0013]–[0014], paragraphs [0084]–[0091] of the published application.

In relation to an enabling disclosure on the utilization of the recognition molecules of the present invention and/or constructs thereof, the Examiner is courteously invited to review the disclosure contained in the Examples of the present application. For example, Example 7, Applicants' specification provides a disclosure of the ability of the recognition molecules to serve as diagnostic tools, for example, in the recognition of core-1 positive tumor cells. See, the disclosure in Figs. 5 and 6 and the description thereof in paragraphs [0160] and [0161] of the published specification. Moreover, the disclosure in Example 13 of Applicants' specification expressly teaches that the constructs of the present invention, such as, for example ^{90}Y-conjugated antibodies, are useful for therapy of tumors.

Although not necessary, enclosed herewith in Exhibit A is a report on the experiments performed by the inventors of the instant application.

The Report shows that the claimed recognition molecule

- affects antibody dependent cell cytotoxicity (ADCC); see Example I;
- affects complement dependent cell cytotoxicity (CDC); see Example II;
- induces apoptosis in tumor cells; see Example III; and
- inhibits proliferation of a human tumor cell line; see Example IV.

These data clearly demonstrate that the claimed recognition molecule is useful for the reduction, therapy and following-up or aftercare of a core 1-positive tumor disease or metastasis. Likewise, it is also useful for the diagnosis of a core 1-positive tumor or metastasis as it binds to core1. As shown above, the claimed recognition molecule can be labeled with a diagnostic reagent (for example, a radioactive label) and, thus, it can be used for diagnostic applications. The arguments and evidence presented for claim 81 are equally applicable to claim 84. In fact, claim 84 refers to the recognition molecule of claim 79 which is the recognition molecule of claim 74 further comprising an additional entity such as a label, enzyme, etc. Accordingly, the recognition molecule referred to in claim 84 has the same properties as that of claim 74 and, thus, it is useful for the claimed medical application.

Thus it is respectfully submitted that the specification provides an enabling disclosure on the claimed end uses of the instant invention. Therefore, the specification's express teaching that the claimed molecules are therapeutically useful is clearly credible. The PTO's contentions regarding non-enablement based on the "unpredictability" and "lack of working examples" are especially weak in view of the detailed disclosure contained in the originally-filed specification, further in view of the corroborating experimental evidence submitted herewith. Withdrawal of the rejection is respectfully requested.

(d) Method of making the recognition molecules

Applicants disagree with the PTO's contention that the use of viruses for making the recognition molecules is non-enabled. However, in order to facilitate prosecution, the claims have been limited to host cell method of production of the instantly claimed recognition molecules. Withdrawal of the rejection is respectfully requested.

Based on the aforementioned remarks and arguments, further in view of the amendments presented herein, it is respectfully submitted that Applicants' specification provides an enabling

disclosure of what is claimed by the present invention. Withdrawal of the rejection under 35 U.S.C. §112, ¶1, is respectfully requested.

Prior art rejection

Claims 74, 75, 77, 78 and 79 are rejected under §102(b) as allegedly anticipated by Karten (*Hybridoma*, 1995).

Reconsideration of this rejection in view of the decisions in *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1306-07 (Fed. Cir. 2006) and *Elan Pharms., Inc. v. Mayo Found. for Med. Educ. & Research* (Fed. Cir. 2003) is respectfully requested. Therein, Courts unequivocally held that "an anticipating reference must be enabling." It is submitted that insofar as Karsten fails to disclose the claimed recognition molecule in an enabling manner, the disclosure therein cannot anticipate the subject matter of the present claims. For example, given Karsten's Abstract, a skilled artisan would not have been able to generate the claimed recognition molecule having the specific heavy and light chain variable regions recited in Applicants' claims. This is because the Karsten's hybridoma was not publicly deposited/available. Moreover, it is not even evident based on the disclosure in the cited abstract that whether the antibody possess the structural (i.e., amino acid sequences) and the functional (i.e., Core-1 binding ability) recited in the claims. Accordingly, this rejection cannot stand.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

No fees are believed to be due with this paper; however, the Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

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